Prospective Multicenter Phase II Study of HLA-Haploidentical Peripheral Blood Stem Cell Transplantation after Reduced-Intensity Conditioning with Post-Transplant Cyclophosphamide: First Analysis of the JSCT Haplo13 Study

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Introduction: HLA-haploidentical bone marrow transplantation using posttransplant high-dose cyclophosphamide (Cy) has been increasingly performed, but relapse remains a major problem. To test whether the addition of busulfan to the conditioning regimen and the use of peripheral blood stem cells (PBSCs) instead of bone marrow could reduce relapse, we conducted a multicenter phase II study to evaluate the safety and efficacy of posttransplant Cy-based HLA-haploidentical peripheral blood stem cell transplantation (PBSCT) after busulfan-containing reduced-intensity conditioning.

Patients and methods: This study started in May 2013 (Trial identifier: UMIN000010316). Patients aged from 15 to 65 with hematological malignancies who were planned for HLA-haploidentical PBSCT were enrolled. The conditioning regimen consisted of fludarabine (30 mg/m2/day on days -6 to -2), Cy (14.5 mg/kg/day on days -6 and -5), busulfan (3.2 mg/kg/day on days -3 and -2) and TBI (2 Gy on day -1). GVHD prophylaxis consisted of Cy (50 mg/kg/day on days 3 and 4), tacrolimus (days 5 to 180), and mycophenolate mofetil (days 5 to 60). Our primary endpoint was the incidence of non-relapse mortality (NRM) at day 100. Secondary endpoints included overall survival (OS), disease-free survival (DFS), the incidence of engraftment, acute GVHD, and relapse.

Results: Median age was 48 (range 21-65) with 22 male and 9 female. Diagnosis of the patients included AML (n=17), ALL/LBL (n=8), MDS/MPN (n=4), and lymphoma (n=2). The majority (61.3%) of patients were not in remission and 13 patients (41.9%) had a history of prior allogeneic stem cell transplantation (allo-SCT). Twenty-seven patients (87.1%) engrafted with median neutrophil engraftment on 19 days (range 15-27). The cumulative incidence of grades II-IV and III-IV acute GVHD at day 100 was 22.6% (95% CI, 9.8-38.6%) and 3.2% (95% CI, 0.2-14.4%), respectively. NRM at day 100 was 19.4% (95% CI, 7.7-34.9%). Cumulative incidence of relapse at day 100 was 19.4% (95% CI, 7.7-35.0%). With a median follow-up of 171 days, OS and DFS was 74.2% (95% CI, 55.0-86.2%) and 61.3% (95% CI, 42.0-75.8%), respectively, at day 100. Subgroup analysis showed that patients who had a history of prior allo-SCT had higher NRM (30.8% vs. 11.1%, p=0.07) and lower OS (53.8% vs. 83.9%, p=0.03) than those in patients without a history of prior allo-SCT.

Conclusions: Our results suggest that posttransplant Cy based HLA-haploidentical PBSCT after busulfan containing reduced-intensity conditioning achieves stable donor engraftment and low incidence of GVHD. NRM was acceptable in the setting of the first allo-SCT. Given the promising results of GVHD and NRM, phase II study in much larger scale are now under investigation.